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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

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Applicant argues that because Verbruggen teaches xylosan polysulfate and chondroitin polysulfate but not heparin, significantly increase aggrecan aggregate sizes, therefore Verbruggen teaches away form using heparin-like molecules interchangeably in chondrocyte cultivation. Applicant argues that Verbruggen concludes that heparin-like molecules have different or unpredictable effects on chondrocyte development (see Remarks page 3 2nd -4th paragraphs filed on 05/04/2010). These arguments are considered but are not found persuasive because Verbruggen et al. do not teach xylosan polysulfate and chondroitin polysulfate are heparin-like molecules (or heparinoids), instead Verbruggen et al. teach xylosan polysulfate, chondroitin polysulfate are polysulphated polysaccharides. Verbruggen et al. teach polysulphated polysaccharides, xylosan polysulfate, chondroitin polysulfate, increased the synthesis of high molecular weight hyaluronan by chondrocyte. Verbruggen et al. further teach stimulation of the production of high molecular weight hyaluronan by chondrocytes seems to be a common effect of polysulfated polysaccharides (p1669 1st column 5th paragraph lines 24-28).

Moreover, Verbruggen et al. teach polysulphated polysaccharides, xylosan polysulfate and chondroitin polysulfate, consistently improved aggrecan synthesis in the culture chondrocytes, and heparin was less active on these cells (page 1669 1st column 4th paragraph lines 1-4). Therefore, Verbruggen et al. neither teach away form using heparin (or heparin-like molecules) in chondrocyte cultivation nor concludes that heparin-like molecules have unpredictable effects on chondrocyte development, as alleged by the Applicant.

Applicant argues that one of ordinary skill in the art would have not been motivated to combine Verbruggen and Rosenberg teachings and that the combination of references fails to provide a motivation to use polysulphated alginate for chondrocyte cultivation (see Remarks page 3 4th paragraphs filed on 05/04/2010).These arguments are considered but are not found persuasive because Rosenberg et al. teach polysulfates prepared from alginic acid (polysulphated alginate) and chondroitin polysulphates are polysulfated polysaccharides, which are non-thrombogenic (heparin-like effect). Rihova teach a matrix suitable for implantation, must be non-thrombogenic (anticoagulant activity) to be biocompatible. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to try (choosing form a finite number of identified polysulfated polysaccharides) and to use polysulfated polysaccharide, polysulphated alginate, in the method and the composition as taught by Verbruggen et al. with a reasonable expectation of success in providing an in vitro method for cultivation of chondrogenic cells, a composition comprising polysulphated alginate, and a method of treatment of cartilage defects. The motivation as taught by Verbruggen et al. would be stimulation of the production of high molecular weight hyaluronan by chondrocytes seems to be a common effect of polysulfated polysaccharides.